

**WHAT IS CLAIMED IS:**

1. A method for detecting the presence of anti-folate receptor (FRs) autoantibodies in a biological sample of a subject comprising:
  - a. acidifying said biological sample to a pH about 3.0 to pH about 5.0 to generate apo-FRs in said biological sample by dissociating anti-FRs autoantibodies and endogenous folate bound to said FRs,
  - b. removing the dissociated folate,
  - c. incubating said biological sample with labeled folic acid (FA) at a pH about 8.0 to pH about 8.9,
  - d. incubating said biological sample from Step c with labeled purified FRs, and
  - e. detecting and quantifying the formation of an immune complex between said anti-FRs autoantibodies present in said biological sample and said labeled purified FRs or previously labeled apo-FRs, wherein the presence of said immune complex indicates that said subject has anti-FRs autoantibodies.
2. A method for detecting the presence of an autoantibody that blocks the binding of folate to FRs in a biological sample from a subject, comprising:
  - a. obtaining a FRs-bound matrix ,
  - b. dissociating folate bound to the FRs on said matrix and generating apo-FRs on said matrix by acidifying said matrix at a pH about 3.0 to pH about 5.0,
  - c. washing said matrix in the acid buffer to remove the dissociated folate from Step b,
  - d. resuspending said matrix in buffer, at a pH about 7.0 to pH about 8.6, and determining the folate binding capacity per unit volume by the binding of labeled folic acid,
  - e. removing free folate from said biological sample,
  - f. obtaining a control sample, and removing free folate from said control sample,

- g. incubating the suspended matrix from Step d with said biological sample from Step e in a buffer with a pH about 7.0 to pH about 8.6,
- h. incubating the suspended matrix from Step d with said control sample from Step f, in a buffer with a pH of about 7.0 to 8.6,
- 5 i. washing said matrix from Step g and Step h,
- j. incubating said matrix from Step i with labeled folic acid,
- k. determining and quantifying the labeled folic acid binding capacity to said matrix from Step g and to said matrix from Step h, whereby a reduction of said labeled folic acid binding to said matrix in Step
- 10 g compared to said labeled folic acid binding to said matrix from Step h indicates the presence of autoantibodies that block the binding of folate to FRs in said subject.
3. The method of Claims 1 and 2, wherein said subject is human.
4. The method of Claims 1 and 2, wherein said biological sample is serum.
- 15 5. The method of Claims 1 and 2, wherein said FRs are detectably labeled.
6. The method of Claim 1, wherein said immune complex is detected by formation of a second immune complex between said immune complex of Claim 1 and an immunoglobulin-binding agent.
7. The method of Claim 6, wherein said immunoglobulin-binding agent is a
- 20 protein A membrane suspension.
8. The method of Claim 6, wherein said immunoglobulin-binding agent is a detectably labeled second antibody
9. The method of Claim 1, wherein said immune complex is detected by precipitating said immune complex using ammonium sulfate, sodium sulfate, alcohol,
- 25 or polyethylene glycol.
10. The method of Claim 2, wherein said matrix is placental membrane containing FRs from a human or homologous species.
11. A test kit for detecting autoantibodies to FRs in a biological sample from a subject comprising purified FRs from a human or homologous species, reagents for
- 30 treating said biological sample, labeled folic acid, and at least one indicator which detects a complex of said purified FRs and said autoantibodies.

12. A test kit for detecting autoantibodies to FRs that block the binding of folate by the FRs in a biological sample from a subject comprising apo-FRs from a human or homologous species, reagents for treating said biological sample, labeled folic acid, and at least one indicator which detects said apo-FRs remaining in the  
5 reaction.

13. The test kit of Claims 11 and 12, wherein said kit can also determine the titer of said blocking autoantibody.

14. The test kit of Claims 11 and 12, wherein said kit can also determine the apparent association constant ( $K_a$ ) of said blocking autoantibody to said FRs.

10 15. The test kit of Claims 11 and 12, wherein said FRs are bound to a matrix.

16. The test kit of Claim 15, wherein said matrix is a hydrophobic matrix.

17. The test kit of Claim 15, wherein said matrix is placental membrane containing FRs from a human or homologous species.

15 18. The test kit of Claims 11 and 12, wherein said indicator is selected from the group consisting of enzyme, radioactive label, fluorescent marker, or biotin.

19. A method for diagnosing a folate-sensitive abnormality or disorder in a subject at risk of said abnormality or disorder comprising the detection of the presence of autoantibodies to FRs in a biological sample according to the methods of Claim 1 or 2.

20 20. A method for screening a woman at risk for having a neural tube defect-complicated pregnancy comprising detecting the presence of maternal autoantibodies to the FRs in a biological sample from said woman according to the methods of Claim 1 or 2.

25 21. A method for the prevention of folate-sensitive abnormalities or disorders in a subject comprising:

a. detecting the presence of autoantibodies to FRs in a biological sample from the subject according to the methods of Claim 1 and 2, and

b. administering pharmacologic folate supplements to the subject.

30 22. The method of Claims 19-21, wherein said folate-sensitive abnormality or disorder is selected from the group consisting of neural tube defects (NTDs),

infertility, spontaneous abortion, male sterility, unsuccessful *in vitro* fertilization, neurologic disorders and impaired intestinal folate absorption.